**Review Article**

**A Review on *Terminalia chebula* *Retz* Fruit: A Treasure trove of Phytochemicals & Therapeutic Potential**

**Abstract**

*Terminalia chebula* stands out as a plant of significant therapeutic promise, deeply rooted in traditional medicine and increasingly validated by modern scientific inquiry. Its wide geographical distribution and adaptability have contributed to its long-standing use across diverse cultures, while its rich phytochemical profile, brimming with phytochemicals such as flavonoids, alkaloids, polyphenols, and triterpenoids, forms the basis of its multifaceted pharmacological activities. This review encompasses researches demonstrating *T. Chebula* efficacy in addressing a spectrum of health challenges. From its potent antioxidant and anti-inflammatory effects, which underpin its benefits in various chronic diseases, to its promising anticancer, antimicrobial, cardioprotective, antidiabetic, and hepatoprotective potential. The exploration of *T. Chebula* mechanisms of action reveals a complex interplay of cellular pathways, highlighting the intricate nature of its therapeutic approach and linking the gap between traditional wisdom and modern medicine. This review will not only build up our understanding of *T. Chebula* therapeutic potential but also cover the way for developing novel, evidence-based therapeutic strategies, leveraging the rich legacy of this remarkable medicinal plant.

**Keywords: -** *T. Chebula* Efficacy, Therapeutic Potential, Phytochemicals, Medicinal Plant.

1. **Introduction**

*Terminalia chebula* Retz., a member of the *Combretaceae* family, is a well-known medicinal plant found across India, Myanmar (formerly Burma), and Sri Lanka. For centuries, conventional Indian medicine systems have relied on a vast array of indigenous plants to combat various illnesses and infections. *T. Chebula* holds a particularly well-known place surrounded by these systems, normally used as a key ingredient in traditional remedies. It's so highly regarded that it's often referred to as the "King of Medicine”. In Ayurvedic *T. Chebula* consistently ranks at the top, a testament to its exceptional healing capabilities. This widespread use and reputation have spurred significant scientific interest in the plant *(Basha et al., 2017)*. *Terminalia chebula* Retz., particularly its dried fruit known as *chebulae* Fructus, is of medicinal value with a long and globally recognized history. The therapeutic uses of fruits were first documented as far back as the Jin Dynasty. Researchers have identified around 149 different compounds in the plant, including tannins, phenolic acids, lignins, triterpenes, flavonoids, and volatile compounds. Those compounds are in charge of a wide range of biological activities observed in laboratory and animal studies, such as antioxidant, anti-inflammatory, antiviral, anticancer, antibacterial, liver-protecting, kidney-protecting, nerve-protecting, and anti-diabetic effects. Some of these certain positive aspects are already being used in clinical settings. However, although significant progress been made, studies need to focus on how it works, how the body handles it, and its complete safety profile, both for the extracts and the individual compounds *(Wang C. et al., 2024).*

This review aims to bring together the findings of various pharmacological and biochemical studies conducted on *Terminalia chebula*. Furthermore, we will explore not only its conventional uses and also the evidence that is based on facts supporting its efficacy, potentially opening avenues for its combination into modern healthcare application and highlighting its importance in promoting well-being. We will also examine the chemical components responsible for its diverse pharmacological activities, providing a clearer picture of its medicinal value. This review brings together the latest information on *chebulae* Fructus, covering its traditional uses, chemical makeup, pharmacological properties, potential toxicity, and how the body processes it (pharmacokinetics). We emphasize its clinical importance and the promising therapeutic potential of its various components.

This review indicates a strong desire for more research in these areas to fully unlock the therapeutic potential of *chebulae* Fructus and make it easier to use in clinical practice. This detailed investigation not only confirms the significance of *chebulae* Fructus in traditional medicine but also sets the platform for upcoming research into its medicinal properties.

1. **Plant Taxonomy: Descriptions and Habitats *(****Khan M. U. et al., 2015****)***

The taxonomy of *Terminalia chebula* Retz. is as follows:

* **Kingdom:** Plantae
* **Sub Kingdom:** Tracheophyta (vascular plants)
* **Class:** Magnoliopsida (dicotyledons)
* **Order:** Myrtales
* **Family:** Combretaceae
* **Genus:** *Terminalia*
* **Species:** *Terminalia chebula*



Picture 1- *Terminalia chebula*

**Some common names:**

* Chebulic Myrobalan
* Black Myrobalan
* Haritaki (Sanskrit)
* Harad (Hindi)
* Kadukkai (Tamil)

  

Picture 2- Dried *Terminalia chebula*

*Terminalia chebula* is a moderately sized to large tree that loses its leaves seasonally (deciduous). Originating in South Asia, it's a prominent plant in traditional medicine, especially in systems like Ayurveda, Unani, and Siddha. People primarily use the fruit of this tree for medicinal purposes*.*

1. **Phytochemical Profile/Characterization**

Plants produce phytochemicals to defend themselves from predators, diseases, and harsh environments. While it is not essential for human existence, these compounds may offer health benefits when consumed. *Terminalia chebula* dried fruits are a source of various phytochemicals. *Terminalia chebula* fruits are a powerhouse of bioactive molecules, specifically phenolics, which contribute significantly to their therapeutic potential. These fruits abound in various phenolic compounds, as well as phenolic acids, tannins, and flavonoids, each offering unique health benefits. Phenolic acids, namely gallic acid, ellagic acid, along with hydroxycinnamic acids, are well-known for their potent antioxidant along with anti-inflammatory properties, keeping cells save from damage and helping to avoid chronic diseases. Tannins, particularly hydrolyzable tannins like terflavin A, terchebulin, punicalagin, chebulagic acid, chebulinic acid, and corilagin, are rich in *T. Chebula* fruits. These compounds show astringent properties, aiding in wound healing and reducing inflammation. They also act as antioxidant and antimicrobial activities, further enhancing the health benefits of *T. Chebula* *(Nigam M. et al., 2020).*

Flavonoids, including rutin, quercetin, and methylated derivatives of quercetin, are another class of the phenolics that are inside in *T. Chebula* fruits. These compounds are recognized for their antioxidant, anti-inflammatory, and anticancer properties, contributing to the prevention of chronic diseases. In addition to phenolic compounds, *T. Chebula* fruits are also an excellent source of vitamin C (ascorbic acid), a well-known antioxidant that strengthens the immune system and protects against infections. The specific composition and concentration the amount of these active compounds depend on factors such as the variety of *T. Chebula*, how is grown, and extraction methods. However, the presence of these diverse compounds in significant amounts makes *T. Chebula* fruits a valuable natural resource for promoting health and preventing diseases. Studies are still being done to understand the therapeutic potential of *T. Chebula* and its various bioactive compounds. However, the information we have now indicates that these fruits could be really helpful for overall health and well-being *(R. Ashwini et al., 2011; Raju D et al., 2009).*

*Terminalia* plants have diverse chemical compositionincluding alkaloids, flavonoids, amino acids, tannins, sterols, fructose, resin, fixed oils, anthraquinones, gallic acid, and chebulagic acid, ellagic and ethaedioic acid, 4,2,4 chebulyl-d-glucopyranose, terpinenes, and terpinenols. It contains more phenolics than other plant extracts. Gallic acid, a major constituent, exhibits hepatoprotective and antioxidant properties. Along with ellagic acid and corilagin, it demonstrates anticancer, antimicrobial, and anti-inflammatory activities. The plant's compounds, including chebulinic acid, tannins, chebulic acid, resin, gallic acid, anthroquinone, and sennoside, contribute for a variety of biological activities. These include antimicrobial, antiviral, anticarcinogenic, antioxidant, adaptogenic, anti-anaphylactic, hypolipidemic, hepatoprotective, cardioprotective, antidiabetic, wound healing, immunomodulatory, and chemopreventive effects *(Ammar Saleem at el., 2002; Bharat Reddy D et al., 2009; Chia Lin Chang and Che San Lin 2012)*. Compounds like 1,2,3,4,6-penta-O-galloyl-b-D-gulcopyranose, chebulagic acid, and chebulinic acid show cytotoxic activity against a variety of human tumor cell lines (A-549, SK-OV-3, SK-MEL-2, XF 389, and HCT15). Chebulagic acid, isolated from *Terminalia chebula*, function as a dual inhibitor of COX-LOX, an antioxidant, and an antitumor agent. It also shows cellular toxicity effects against various cell lines (MDA-MB-231, COLO-205, HCT-15, DU-145, and K-562). The plant is a reliable source of ascorbic acid and various phenols like gallic acid, ellagic acid, tannic acid, β-sitosterol, ethyl gallate, chebulic acid, and mannitol. These compounds can cause apoptosis and necrosis in cells *(Lakshmi Prasad et al., 2006; Ponnusankar S et al., 2011; Pulliah T)*. The fruit of *Terminalia* contains a high percentage (30-32%) of tannins. Tannins are crucial in wound healing through mechanisms like free radical chelation, wound contraction, and increased formation of capillary blood vessels and fibroblasts. Other researchers have synthesis diverse compounds from the fruit, including an ellagitannin (chebulin), punicalagin, terflavin-A, shikimic, gallic, tricontanoic and palmitic acids, beta-sitosterol, daucosterol, triethyl ester of chebulic acid, ethyl ester of gallic acid, and a triterpene (chebupentol). The antiradical activity of the plant is attributed to compounds like phloroglucinol, pyrogallol, ferulic acid, p-vanillic acid, p-coumaric acid, and caffeic acid. The plant contains carbohydrates such as glucose, sorbitol, fructose, sucrose, gentiobiose (in smaller amounts), and traces of arabinose, maltose, rhamnose, and xylose *(Choudhary GP; Archana Srivastava et al., 2010; Phattarakorn Rangsriwong et al., 2009; Mahesh R and Hazeena Begum 2007)*.

1. **Extraction Methodologies**

Researches employ a variety of extraction methodologies to access *T. Chebula*’s medicinal potential, scientists used diverse extraction methods.

**4.1 Soxhlet Extraction Method**

To isolate compounds from *T. Chebula*, researchers utilized a sequential Soxhlet extraction method. Dried fruit powder was used with different solvents like ethyl acetate, acetone, methanol, and water, in this order, reflecting increasing polarity. Solvent was removed by rotary evaporation, followed by lyophilization, yielding dried extracts. These extracts were then stored at 4°C for subsequent analysis. This process yielded fractions based on solvent polarity. *(Singh D. et al., 2014)*

**4.2 Alcoholic & Aqueous Extraction Method**

Dual extraction methods were used on *T. Chebula* dried fruit powder. First, 100g portions were twice subjected to overnight stirring in 75% methanol, followed by centrifugation. The resulting supernatants were combined and vaporized under reduced pressure, after reconstituted in water for biological assays. Second, a separate 100g portion of fine powder was stirred in eight parts of heated distilled water for two hours. The liquid was filtered, concentrated by rotary evaporation, after that spray-dried, yielding- a dry powder. Concentrations of these extracts are expressed in micrograms per milliliter. (*Muhammad S. 2012; Naik GH et al., 2004; Sabu MC and Ramadasan K 2002)*

**4.3 Cold Maceration Extraction Method**

To get extracts from *T. Chebula* dried fruit, a simple cold extraction procedure was followed. 100 grams of powdered fruit peel was soaked in 500 milliliters of ethanol for two days at moderate temperature. After this soaking period, filtered the liquid to extract the plant material. The remaining liquid was then left to dry naturally in the air, leaving behind a residue. This residue, carefully labeled, was collected and stored for future experiments *(Agith P. and Prabha P. S. 2024).*

1. **Nanoparticle Synthesis**

Nanotechnology creates nanoparticles (NPs) by shrinking metals to atomic dimensions. There are several ways to make NPs: **Physical methods** avoid solvent contamination but require a lot of energy for heating and cooling, making them expensive. **Chemical methods** use chemicals to create stable, pure NPs, but these chemicals can contaminate the final product. **Biological methods**, or 'green synthesis,' are trending because they are environmentally friendly. They use natural reducing agents like bacteria, fungi, or plant extracts. Biological synthesis is preferred because it avoids harsh chemicals and high-energy processes. Using plant extracts for NP synthesis is particularly promising for large-scale production and medical applications (*Ramanathan S. et al., 2020)*.

Nature provides ways to create tiny inorganic materials, inspiring a new field of research: biological nanoparticle synthesis. This 'green synthesis' aligns with environmentally friendly chemistry, using safe, non-toxic materials. Biological methods offer a simple, one-step process, resulting in nanoparticles with varied properties, good stability, and controlled sizes. These methods are a valuable alternative to traditional chemical, physical, and hybrid techniques for nanoparticle creation *(Mohanpuria P et al., 2008; Tiwari D. K. et al., 2008; Luechinger N. A. et al., 2010)*.

Nanoparticle fabrication encompasses a spectrum of methodologies, broadly categorized as physical and chemical. Physical techniques, such as plasma arcing, ball milling, thermal evaporation, spray pyrolysis, and lithographic patterning, rely on top-down or bottom-up assembly strategies. Conversely, chemical synthesis, employing modalities like chemical solution deposition, sol-gel processes, and wet chemical reduction, leverages controlled chemical reactions. However, both physical and chemical approaches often necessitate the utilization of high-energy inputs and potent reducing and stabilizing agents, posing potential environmental and human health risks. Consequently, biogenic nanoparticle synthesis, characterized by a single-step bio-reduction mechanism, emerges as a more sustainable alternative, minimizing energy consumption and promoting eco-compatibility.

Green nanobiotechnology offers a compelling alternative for creating stable, biocompatible nanoparticles. Typically, this involves using dried plant material as a reducing agent and a metal salt as the precursor. Silver, with its long-established medicinal and preservative properties, is a common target. These biological syntheses follow a 'bottom-up' approach, relying on natural reducing and stabilizing agents. The process generally involves three key decisions: selecting a suitable solvent, choosing an environmentally safe reducing agent, and employing a non-toxic capping agent to ensure nanoparticle stability *(Narayanan K. B. and Sakth Ivel N. 2011; Singh M. et al., 2011).*

The advantages green synthesized NPs revolutionize drug delivery due to their size and biodegradability. Their small size enables deep tissue penetration and cellular uptake, maximizing drug accumulation at target sites. Utilizing biodegradable materials allows for prolonged, controlled drug release, lasting days or weeks. These properties combined make nanoparticles highly effective for targeted and sustained therapeutic delivery *(Shinde N. C., 2012; Parveen K. et al., 2016)*.

1. **Pharmacological & Therapeutic Efficacy**

**6.1 Anticancer Activity**

Cancer, primary mortality cause worldwide, is characterized by uncontrolled cell proliferation. While advancements in cancer treatment exist, a definitive cure remains elusive, prompting research into natural anticancer agents. *Terminalia chebula* (CF) extracts have demonstrated significant anticancer effects against various tumor cell lines, including breast, colon, melanoma, prostate, and lung cancers, both *in vitro* and *in vivo*. Studies highlight the potent anticancer activity of ethanolic CF extracts, particularly against breast cancer, through mechanisms like HDAC (Histone deacetylase) inhibition and anti-oxidative stress reduction, with effective concentrations showing no adverse effects on normal cells. Methanolic extracts have also exhibited strong *in vitro* cytotoxic effects against multiple human cancer cell lines. Specific compounds isolated from CF, such as corilagin, gallic acid, and ellagic acid, have shown promise against breast cancer. Corilagin induces apoptosis in breast cancer cell lines through Reactive oxygen mediated (ROS)-mediated mechanisms. Gallic acid inhibits metastatic features in breast cancer cells under acidic conditions by downregulating the PI3K/Akt pathway. Ellagic acid reduces cancer cell colonization and promotes apoptosis by inhibiting CDK6 expression. Other CF-derived compounds, like 1,2,3,4,6-penta-O-galloyl-β-D-glucose, induce apoptosis in liver cancer cells *via* the p53 pathway. Corilagin also exhibits anti-cervical cancer properties by promoting apoptosis through the PI3K/AKT and MAPK pathways. Chebulagic acid inhibits AURKA expression and the AURKA/β-catenin/Wnt pathway, suppressing gastric cancer cell tumorigenicity. Collectively, these findings suggest CF's potential as a novel therapeutic agent for various cancer types *(Bishayee A. and Sethi G., 2016; Jabbari N. et al., 2022)*.

**Table 1. Different cancer cell lines used in *T. chebula* fruit extract.**

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| --- | --- | --- | --- |
| S. No. | Cell Lines | Research | Reference |
| 1. | MDA-MB-231(Breast Cancer) | Using CO2 extraction, examined the influence of *Terminalia chebula* fruit extract on MDA-MB-231 breast cancer cells. The findings revealed that the CO2 extract of *Terminalia chebula* fruit **effectively inhibited the growth of MDA-MB-231 cells**. | *(G. B. and E. M. 2016)* |
| 2 | MCF-7(Breast Cancer) | *Terminalia chebula* fruit extract is cytotoxic to breast adenocarcinoma, MCF7 cell lines and is non-hemolytic and thus, the bioactive compounds from the fruit can be used as a **potential therapeutic agent for breast cancer, warranting further in vivo studies and clinical trials**. | *(Venkata S. K. et al., 2018)* |
| 3 | HOS-1 (Osteosarcoma) | *Terminalia chebula* extract has been investigated for its effects on human osteosarcoma cells, specifically the HOS-1 cell line, to understand how it impacts their growth. **Studies indicate that *T. chebula* fruit extract can inhibit cell proliferation and induce cell death in HOS-1 cells**, suggesting a potential anticancer effect. | *(M. R., and C. S., 2018)* |
| 4 | PC-3(Prostate Cancer) | In this research it has been examined how *Terminalia chebula* fruit extract affects prostate cancer cells. **It focuses on the extract's impact on cell survival and growth, seeking to understand its potential therapeutic role.** | *(Hanan N. A. et al., 2018)* |
| 5 | A549(Lung Cancer) | The ethanolic extract, rich in phenolics, triterpenoids, and flavonoids (478 ± 2.2 mg GAE/g and 538 ± 1.4 mg QE/g), showed **greater cytotoxicity against A549 cells,** likely because of its high phenolic and flavonoid content. | *(Hanan N. A. et al., 2018)* |

**6.2 Antioxidant Activity**

*Terminalia chebula* (CF), a fruit traditionally used in Himalayan medicine and diets, has been extensively studied for its potent antioxidant activity. Oxidative stress, an imbalance between reactive oxygen species (ROS) and antioxidants, damages cell and contributes to chronic diseases like cancer, diabetes, cardiovascular disease, and atherosclerosis. The search for natural antioxidants, driven by the side effects of synthetic alternatives, has highlighted CF's potential in phytotherapy. Research has identified polyphenols as key to CF's antioxidant capacity, with *in vitro* assays demonstrating its ability to scavenge free radicals like DPPH, nitric oxide, and hydrogen peroxide. Studies correlate phenolic and flavonoid concentrations in CF extracts with antioxidant activity, noting that different extraction methods yield varying concentrations of active compounds. CF's antioxidant activity stems from its electron-donating phenolic compounds, particularly the abundance of hydroxyl and carboxyl groups, which facilitate free radical scavenging and contribute to both antioxidant and anti-inflammatory effects. Specific compounds like chebulagic acid, chebulinic acid, gallic acid, and ellagic acid, contribute to CF's antioxidant properties through mechanisms like ROS scavenging, iron chelation, and modulation of antioxidant enzyme activity. For example, gallic acid protects against renal toxicity by increasing glutathione levels and boosting antioxidant enzyme activity, while ellagic acid inhibits lipid peroxidation. CF's rich composition of these bioactive compounds positions it as a promising natural antioxidant source with potential therapeutic applications against oxidative stress and related diseases *(Chang C. L. and Lin C. S., 2012; Lee H. S. et al., 2005)*.

**6.3 Antibacterial Activity**

*Terminalia chebula* (CF) exhibits broad-spectrum antibacterial activity against various Gram-positive and Gram-negative bacteria. CF extracts have demonstrated inhibitory effects against several strains, including *Helicobacter pylori*, *Xanthomonas*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, and *Streptococcus mutans*. Ethanolic CF extracts have shown activity against *Enterococcus faecalis*, with antibacterial efficacy increasing with concentration. Different extracts, including ethyl acetate, methanol, and aqueous, inhibit *Porphyromonas gingivalis*, with the ethyl acetate extract, containing a wider range of phytochemicals, exhibiting superior activity. Ethanol extracts also possess anti-caries properties by inhibiting glucan formation and *Streptococcus mutans* at minimally cytotoxic concentrations, suggesting potential use in oral hygiene products. CF extract and its constituent phenolic acid, corilagin, inhibit *Staphylococcus aureus* biofilm formation, potentially by downregulating quorum sensing genes. Ellagic acid has shown promise against drug-resistant bacteria like MRSA, *Pseudomonas aeruginosa*, and *Escherichia coli*. While these findings are promising, further research is needed to elucidate the specific mechanisms of CF's antibacterial action and confirm its efficacy in clinical settings through rigorous scientific studies and clinical trials *(Kannan P. 2009; Zainab G. A. et al., 2022)*.

**6.4 Antiviral Activity**

*Terminalia chebula* (CF) has demonstrated antiviral activity against several viruses, including SARS-CoV-2, influenza A (IAV), herpes simplex virus-1 (HSV-1), and HIV-1. Given the impact of the COVID-19 pandemic, CF's potential against SARS-CoV-2 is of particular interest. Several Chinese medicines containing CF have been approved for use against COVID-19. Aqueous CF extracts inhibit SARS-CoV-2 replication by targeting the viral 3CLpro enzyme. Chebulagic acid and punicalagin also inhibit SARS-CoV-2 replication by acting as allosteric regulators of 3CLpro. Additionally, 1,2,3,4,6-penta-O-galloyl-β-D-glucose inhibits SARS-CoV-2 3CLpro, and corilagin, a non-nucleoside inhibitor, targets the viral RdRp. While promising, *in vivo* further studies are necessary to prove safety and efficacy. CF extracts, punicalagin, and ellagic acid have shown efficacy against IAV, inhibiting viral release and mitigating cytopathic effects by targeting the neuraminidase enzyme. Chebulagic and chebulinic acids are also potential IAV neuraminidase inhibitors. CF extracts and its compounds, including punicalagin and chebulagic acid, have also shown inhibitory effects against HSV-1 and HSV-2 by interfering with viral entry. Chebulinic and chebulagic acids exhibit potent antiviral effects against HSV-2, surpassing acyclovir's efficacy. Finally, CF contains HIV-1 integrase inhibitors, including gallic acid and galloyl glucose derivatives, which inhibit the 3′-processing activity of the enzyme *(Steiner S. et al., 2024; Zhang M. et al., 2023; Chiou W. C. et al., 2022)*.

**6.5 Antidiabetic Activity**

Diabetes, a metabolic disorder marked by insufficient insulin production and resulting hyperglycemia, is often linked to obesity, particularly in type 2 diabetes. *Terminalia chebula* (CF) extracts have shown promise in managing this condition. Aqueous CF extract reduces oxidative stress and increases SIRT1 expression in diabetic rats, demonstrating anti-diabetic effects. Higher CF doses (600 mg/kg) exhibit enhanced anti-diabetic and anti-lipidemic effects, along with pronounced hepatoprotective and Reno protective benefits compared to lower doses. This suggests CF's potential as a standalone or adjunctive therapy for diabetes management. Chebulinic acid, a CF-derived compound, has been identified as a potential anti-diabetic agent targeting both PTPN9 and PTPN11. Studies indicate that chebulinic acid acts as a dual allosteric inhibitor, strongly binding to both enzymes with nanomolar IC50 values. This inhibitor interacts synergistically with both enzymes, enhancing glucose uptake in adipocytes and muscle cells by activating the AMPK signaling pathway. These findings support chebulinic acid's potential as a therapeutic agent for type 2 diabetes *(Wang C. et al., 2024)*.

**6.6 Cardioprotective Activity**

*Terminalia chebula* (CF) demonstrates cardioprotective activity, particularly in isoproterenol-induced cardiac injury models in rats. Isoproterenol, a synthetic catecholamine, can induce myocardial infarction by increasing oxidative stress and lipid peroxidation, damaging cardiac tissue. CF's cardioprotective effects are evident in its ability to mitigate isoproterenol's impact on lipid peroxide production. By reducing lipid peroxidation, CF helps preserve the integrity of cardiac cell membranes and subcellular structures, minimizing cellular damage. Furthermore, isoproterenol typically elevates the levels of diagnostic marker enzymes, such as creatine kinase (CK), lactate dehydrogenase (LDH), and aspartate aminotransferase (AST), in the bloodstream, indicating myocardial damage. CF administration helps maintain the activities of these diagnostic marker enzymes closer to normal levels, suggesting a protective effect against isoproterenol-induced cardiac injury. This preservation of enzyme activity reflects CF's ability to protect the heart muscle from cellular damage and maintain its functional integrity. These combined effects on lipid peroxidation and diagnostic marker enzymes highlight CF's potential as a cardioprotective agent *(Sucha Latha S. and Shyamala Devi, C. S. 2004)*.

**6.7 Antiprotozoal Activity**

*Terminalia chebula* (CF) exhibits antiprotozoal activity against certain parasitic protozoa. Specifically, an acetone extract derived from CF seeds has demonstrated anti-plasmodial action against *Plasmodium falciparum*, the causative agent of malaria. This suggests that CF seed extracts contain compounds capable of inhibiting the growth or survival of the malaria parasite. The exact mechanisms by which CF exerts its anti-plasmodial effects they need more investigation, yet they likely involve targeting essential metabolic pathways or cellular processes within the parasite. In addition to its anti-malarial potential, CF also displays antiamoebic activity. Studies in rats with experimental caecal amoebiasis, an infection caused by the protozoan parasite *Entamoeba histolytica*, have shown a significant 89% reduction in amoebic activity. This indicates that CF extracts possess compounds effective in combating *E. histolytica* infections, potentially by disrupting the parasite's cellular functions or directly killing the amoebae. While these findings highlight CF's potential as a source of antiprotozoal agents, there’s a need for more research is crucial to isolate and identify the key active component that’s behind for these effects, elucidate their mechanisms of action, and evaluate the benefits and safety of them in clinical settings *(Bagavan A. et al., 2011)*.

**6.8 Anti-Inflammatory Activity**

*Terminalia chebula*, also called Haritaki, exhibits significant anti-inflammatory properties, as demonstrated in various studies. A polyherbal formulation containing Haritaki, known as Aller-7, has shown promising results in inhibiting Freund's adjuvant-induced arthritis in rats. This inhibition occurs in a dose-dependent manner, indicating that higher doses of the formulation correlate with greater anti-inflammatory effects. Freund's adjuvant induces a robust inflammatory response, mimicking certain aspects of rheumatoid arthritis, making it a useful model for studying anti-inflammatory agents. The mechanism by which Haritaki exerts its anti-inflammatory action involves the inhibition of inducible nitric oxide (iNOS) production. Nitric oxide (NO) is essential for inflammation, and iNOS is an enzyme provides a significant supply of NO at inflammatory sites. By inhibiting iNOS, Haritaki effectively reduces NO production, thus dampening the inflammatory cascade. This reduction in NO production contributes to the observed decrease in arthritis severity in the rat model. These findings suggest that Haritaki, particularly as a constituent of Aller-7, holds potential as a pharmaceutical agent for inflammatory conditions, possibly by modulating NO production through iNOS inhibition. More investigation is required to truly elucidate the key active elements that are behind this effect and to evaluate its efficacy and safety in human clinical trials *(Moeslinger T. et al., 2000; Jha A. K. and Sit N. 2023)*.

**6.9 Antiarthritic Activity**

Chebulagic acid, a compound extracted from the immature seeds of *Terminalia chebula*, has demonstrated promising antiarthritic activity in rat models. Studies using collagen-induced arthritis, a widely used model mimicking rheumatoid arthritis, have shown that chebulagic acid effectively inhibits both the development and progression of the disease. This suggests that chebulagic acid may possess both preventative and therapeutic potential against arthritis. The precise mechanisms by which chebulagic acid exerts its antiarthritic effects are still under investigation, but it likely involves modulation of the inflammatory cascade and immune response. Inhibition of pro-inflammatory cytokines, reduction of cartilage degradation, and suppression of autoantibody production are potential pathways through which chebulagic acid may exert its beneficial effects. These findings suggest that chebulagic acid, derived from *Terminalia chebula*, holds promise as a potential therapeutic agent for arthritis, although further research, including clinical trials, is necessary to confirm its efficacy and safety in humans *(Jha A. K. and Sit N. 2023)*.

**6.10 Other Medicinal Activity**

*Terminalia chebula* (Haritaki) has a long history of traditional use for various ailments. Combined with sugar water, it's been used for ophthalmia, skin irritation, and edema. Its preparations have also addressed heart problems, brain dysfunction, and inflammation, acting as both an antioxidant and neuroprotective agent, and aiding in stress recovery. Chebulagic acid, a component of Haritaki, exhibits antispasmodic activity comparable to papaverine. The plant has even been used as a snake bite antidote. Haritaki is believed to enhance memory by supporting brain nerves and acts as an adjuvant herb in chronic fever. Interestingly, its long-term use can both increase and decrease body weight depending on individual needs. It can also help control hemorrhage. Consumed before meals, it aids digestion; taken with meals, it's thought to boost brainpower, nurture senses, and disinfect the gastrointestinal and genitourinary tracts. Haritaki improves digestion, regulates colon function, and enhances nutrient absorption. Its adrenergic properties contribute to stress management. The presence of a brown dye powder and chebulinic acid helps eliminate toxins and unwanted fat. It's also used to improve skin glow and complexion, and its ethanolic fruit extract has demonstrated efficacy in protecting skin from photodamage. Finally, recent studies have investigated the antidiarrheal properties of its fruit's aqueous extract, aiming to identify the active fraction responsible for this effect *(Kolla J. N. et al., 2017)*.



**Fig. 1. *T. chebula* Dried Fruit Pharmacological & Therapeutic Properties**

1. **Conclusion**

In conclusion, *Terminalia chebula* emerges from this review as a plant of significant therapeutic promise. This review has synthesized a wealth of research demonstrating *T. chebula*'s efficacy in addressing a spectrum of health challenges. While preclinical studies have demonstrated significant promise, rigorous clinical trials are essential to establish the safety and efficacy of *T. chebula* extracts and isolated compounds in humans. Standardized extraction and purification methods are crucial for ensuring consistent quality and potency of *T. chebula*-based products. Further research should focus on identifying the specific bioactive components responsible for each observed therapeutic effect and elucidating their precise mechanisms of action at the molecular level. Investigating synergistic interactions between different phytochemicals within *T. chebula* extracts could lead to the development of more effective multi-target therapies. Exploring novel delivery systems for these bioactive compounds, such as nanoparticles or liposomes, could enhance their bioavailability and improve therapeutic outcomes. Additionally, studies on the long-term effects and potential toxicity of *T. chebula* extracts are necessary to ensure safe and sustainable use. Integrating traditional knowledge with cutting-edge research techniques, including genomics, proteomics, and metabolomics, can provide a deeper understanding of *T. chebula*'s therapeutic potential. Finally, sustainable harvesting practices and conservation efforts are crucial to protect this valuable resource and ensure its availability for future generations. By combining scientific rigor with respect for traditional knowledge, *T. chebula* can be further developed into a powerful tool for promoting human health and well-being.

1. **References**
	1. Ajith, P., & Prabha, P. S. (2024). Biological Activity of Ethanol Extract of *Terminalia chebula* Dried Carp against Bacterial Wilt of Lycopersicum esculentum and its Mechanism of Inhibition. *Indian Journal of Pharmaceutical Education and Research*, *58*(4), 1157–1166. <https://doi.org/10.5530/ijper.58.4.127>
	2. Akbari, F., Azadbakht, M., Gaurav, A., Azimi, F., Mahdizadeh, Z., Vahedi, L., Nejad, A. B., Chabra, A., & Eghbali, M. (2022). Evaluation of the therapeutic effect of the traditional herbal medicine atrifil and oshagh gum on Testosterone-Induced benign prostatic hyperplasia in Wistar rats. *Advances in Urology*, *2022*, 1–14. <https://doi.org/10.1155/2022/5742431>
	3. Ammar Saleem , Michael Husheem , Pirkko Ha¨rko¨nen , Kalevi Pihlaja, Inhibition of cancer cell growth by crude extract and the phenolics of *Terminalia chebula* retz. Fruit, Journal of Ethnopharmacology ,81, 2002, 327-336.
	4. Archana Srivastava,, Abhishek Chandra, Madhulika Singh, Farrukh Jamal, Preeti Rastogi, Siron Mani Rajendran, Falgun Wanganuji Bansode, Vijai Lakshmi, Inhibition of hyaluronidase activity of human and rat spermatozoa in vitro and antispermatogenic activity in rats in vivo by *Terminalia chebula*, a flavonoid rich plant, Reproductive Toxicology, 29 , 2010, 214–224.
	5. Bagavan, A., Rahuman, A. A., Kamaraj, C., Kaushik, N. K., Mohanakrishnan, D., & Sahal, D. (2011). Antiplasmodial activity of botanical extracts against *Plasmodium falciparum*. *Parasitology Research*, **108**(5), 1099–1109.
	6. Basha, S. J., Reddy, V. J., Y, S. R., M, K., G, H., & Dadakhalandar, S. (2017). A review on *Terminalia chebula*. *International Journal of Pharmacological Research*, *7*(10), 187–191. <https://doi.org/10.7439/ijpr.v7i10.4431>
	7. Bharat Reddy D, Reddy TCM, Jyotsna G, Satish Sharan, Nalini Priya, Lakshmipathi V, Pallu Reddanna, Chebulagic acid, a COX–LOX dual inhibitor isolated from the fruits of *Terminalia chebula* Retz., induces apoptosis in COLO-205 cell line, Journal of Ethnopharmacology, 124, 2009, 506–512.
	8. Bishayee, A.; Sethi, G. Bioactive natural products in cancer prevention and therapy: Progress and promise. *Semin. Cancer Biol.* **2016**, *40*, 1–3.
	9. Chandil, Shachi et., al. (2021). IN-VITRO STUDY OF CO2 EXTRACT OF TERMINALIA CHEBULA IN BREAST CANCER CELL LINE MD-MB-231. *CELLMED* , *11* (3), 16–16. <https://doi.org/10.5667/CELLMED.2021.0016>
	10. Chang, C.L.; Lin, C.S. Phytochemical composition, antioxidant activity, and neuroprotective effect of *Terminalia chebula* Retzius Extracts. *Evid. Based Complement. Altern. Med.* **2012**, *2012*, 125247.
	11. Chia Lin Chang and Che San Lin, Phytochemical Composition, Antioxidant Activity and Neuroprotective Effect of *Terminalia chebula* Retzius Extracts, EvidenceBased Complementary and Alternative Medicine , Volume 2012, Article ID 125247, 7 pages.
	12. Chiou, W.C.; Chen, J.C.; Chen, Y.T.; Yang, J.M.; Hwang, L.H.; Lyu, Y.S.; Yang, H.Y.; Huang, C. The inhibitory effects of PGG and EGCG against the SARS-CoV-2 3C-like protease. *Biochem. Biophys. Res. Commun.* **2022**, *591*, 130–136.
	13. Choudhary GP, Wound healing activity of ethanolic extract of *Terminalia chebula* Retz., International Journal of Pharma and Bio Sciences, 2(1), 48-52.
	14. Jabbari, N.; Feghhi, M.; Esnaashari, O.; Soraya, H.; Rezaie, J. Inhibitory effects of gallic acid on the activity of exosomal secretory pathway in breast cancer cell lines: A possible anticancer impact. *Bioimpacts* **2022**, *12*, 549–559.
	15. Jha, A. K., & Sit, N. (2023). Methods of extraction of bioactive compounds from*Terminalia chebula*(Haritaki) and their application in food and pharmaceutical industry: A review. *Food Bioengineering*, *2*(2), 139–150. <https://doi.org/10.1002/fbe2.12053>
	16. Kannan, P. Antibacterial activity of *Terminalia chebula* fruit extract. *Acad. J.* **2009**, *3*, 180–184.
	17. Khan M.U., Habibullah, Khalilullah, Jawed Akhtar, Gamalosmanel Hasan. *Terminalia chebula*: an ephemeral glance: International Journal of Pharmacy and Pharmaceutical Sciences 2015; 2(7): 3
	18. Kim, H. L., Choi, B., & Yang, S. H. (2022). Terminalia chebula Medicinal Uses: A Review of in vitro and in vivo Studies. *Biotechnology and Bioprocess Engineering*, *27*(5), 729–739. <https://doi.org/10.1007/s12257-022-0090-0>
	19. Kolla, J. N., Kulkarni, N. M., Kura, R. R., & Theepireddy, S. K. R. (2017). *Terminalia chebula* Retz. – an important medicinal plant. *Herba Polonica*, *63*(4), 45–56. <https://doi.org/10.1515/hepo-2017-0024>
	20. Lakshmi Prasad, Tajdar Husain Khan, Tamanna Jahangir, Sarwat Sultana, Chemomodulatory effects of *Terminalia chebula* against nickel chloride induced oxidative stress and tumor promotion response in male Wistar rats, Journal of Trace Elements in Medicine and Biology, 20, 2006, 233–239.
	21. Lee, H.S.; Won, N.H.; Kim, K.H.; Lee, H.; Jun, W.; Lee, K.W. Antioxidant effects of aqueous extract of *Terminalia chebula* in vivo and in vitro. *Biol. Pharm. Bull.* **2005**, *28*, 1639–1644.
	22. Luechinger N.A, Grass R.N, Athanassiou E.K, and Stark W.J, “Bottom-up fabrication of metal/metal nanocomposites from nanoparticles of immiscible metals,” Chemistry of Materials, 2010, vol. 22, no. 1, pp. 155–160.
	23. Mahesh R, Hazeena Begum V, Effect of *Terminalia chebula* on oxidative stress in the liver of young and aged rats, Indian Journal of Gerontology, 21(2), 2007, 244-256.
	24. Moeslinger, T., Friedl, R., Volf, I., Brunner, M., Koller, E., & Spieckermann, P. G. (2000). Inhibition of inducible nitric oxide synthesis by the herbal preparation Padma 28 in macrophage cell line. *Canadian Journal of Physiology and Pharmacology*, **78**(11), 861–866.
	25. Mohanpuria P, Rana N.K, and Yadav S.K, “Biosynthesis of nanoparticles: technological concepts and future applications,” Journal of Nanoparticle Research, 2008, vol. 10, no. 3, pp. 507–517.
	26. Muhammad, S. (2012). The morphology, extractions, chemical constituents and uses of *Terminalia chebula*: A review. *Journal of Medicinal Plants Research*, *6*(33). <https://doi.org/10.5897/jmpr11.1339>
	27. Naik GH, Priyadarsini KI, Naik DB, Gangabhagirathi R, Mohan H (2004). Studies on the Aqueous Extract of *Terminalia chebula* as a Potent Antioxidant and a Probable Radioprotector. Photomed. 11: 530-538.
	28. Narayanan K.B, and Sakthivel N, “Green synthesis of biogenic metal nanoparticles by terrestrial and aquatic phototrophic and heterotrophic eukaryotes and biocompatible agents,” Advances in Colloid and Interface Science, 2011, vol. 169, no. 2, pp. 59–79.
	29. Nigam, M., Mishra, A. P., Adhikari‐Devkota, A., Dirar, A. I., Hassan, M. M., Adhikari, A., Belwal, T., & Devkota, H. P. (2020). Fruits of *Terminalia chebula*Retz.: A review on traditional uses, bioactive chemical constituents and pharmacological activities. *Phytotherapy Research*, *34*(10), 2518–2533. <https://doi.org/10.1002/ptr.6702>
	30. Parveen, K., Banse, V., & Ledwani, L. (2016). Green synthesis of nanoparticles: Their advantages and disadvantages. *AIP Conference Proceedings*. https://doi.org/10.1063/1.494516
	31. Phattarakorn Rangsriwong, Nuchanart Rangkadilok, Jutamaad Satayavivad, Motonobu Goto, Artiwan Shotipruk, Subcritical water extraction of polyphenolic compounds from *Terminalia chebula* Retz. Fruits, Separation and Purification Technology, 66, 2009, 51–56.
	32. Ponnusankar S , Subrata Pandit, Ramesh Babu, Arun Bandyopadhyay, Pulok K Mukherjee, Cytochrome P450 inhibitory potential of Triphala—A Rasayana from Ayurveda, Journal of Ethnopharmacology, 133, 2011, 120–125.
	33. Pulliah T, Encycllopedia of world Medicinal Plants, Volume 4, Regency Publications, New Delhi, India, Pg.1931-1934.
	34. R. Ashwini, S. Gajalakshmi, S. Mythili, A. Sathiavelu\* School of Biosciences and Technology, VIT University, Vellore-632014, Tamil Nadu, India. Received on: 19-05-2011; Revised on: 08-06-2011; Accepted on:01-07-2011
	35. Raju D, Ilango K, Chitra V, Ashish K, Evaluation of Anti-ulcer activity of methanolic extract of *Terminalia chebula* fruits in experimental rats, Journal of Pharmaceutical Science and Research, 1(3), 2009, 101-107
	36. Ramanathan, S., Gopinath, S. C., Arshad, M. M., Poopalan, P., & Perumal, V. (2020). Nanoparticle synthetic methods: strength and limitations. In *Elsevier eBooks* (pp. 31–43). <https://doi.org/10.1016/b978-0-12-821163-2.00002-9>
	37. Reddy, P., Pradeep, S., M, G. S., Ramu, R., Kollur, S. P., & Shivamallu, C. (2022). Anti-breast cancer potential of MnO2 nanoparticles using Terminalia chebula fruit extract against MCF-7 cell line through in vitro cell cycle and apoptotic studies. *Materials Today Proceedings*, *62*, 5526–5532. <https://doi.org/10.1016/j.matpr.2022.04.330>
	38. Sabu MC, Ramadasan K (2002). Anti-Diabetic Activity of Medicinal Plants and Its Relationship with Their Antioxidant Property. J. Ethnopharmacol. 81:155-160.
	39. Shankara, B. R., Dhananjaya, B., Ramachandra, Y., Rajan, S., Ganapathy, P. S., Yarla, N., & Richard, S. (2016). Evaluating the anticancer potential of ethanolic gall extract of Terminalia chebula (Gaertn.) Retz. (combretaceae). *Pharmacognosy Research*, *8*(3), 209. <https://doi.org/10.4103/0974-8490.182919>
	40. Shinde N.C, Research Journal of Pharmaceutical, Biological and Chemical Sciences. Nanoparticles: Advances in Drug Delivery Systems,2012.
	41. Singh M, Manikandan S, and Kumaraguru A.K, “Nanoparticles: a new technology with wide applications,” Research Journal of Nanoscience and Nanotechnology, 2011, vol. 1, no. 1, pp. 1–11.
	42. Singh, D., Singh, D., Choi, S. M., Zo, S. M., Painuli, R. M., Kwon, S. W., & Han, S. S. (2014). Effect of Extracts of *Terminalia chebula* on Proliferation of Keratinocytes and Fibroblasts Cells: An Alternative Approach for Wound Healing. *Evidence-based Complementary and Alternative Medicine*, *2014*(1). <https://doi.org/10.1155/2014/701656>.
	43. Steiner, S.; Kratzel, A.; Barut, G.T.; Lang, R.M.; Aguiar Moreira, E.; Thomann, L.; Kelly, J.N.; Thiel, V. SARS-CoV-2 biology and host interactions. *Nat. Rev. Microbiol.* **2024**, *22*, 206–225.
	44. Suchalatha, S., & Shyamala Devi, C. S. (2004). Protective effect of *Terminalia chebula* against experimental myocardial injury induced by isoproterenol. *Indian Journal of Experimental Biology*, **42**(2), 174–178.
	45. Tiwari D.K, Behari J, and Sen P, “Time and dose-dependent antimicrobial potential of Ag nanoparticles synthesized by topdown approach,” Current Science, 2008, vol. 95, no. 5, pp. 647–655.
	46. Wang, C., Zhang, H., Wang, X., Wang, X., Li, X., Li, C., Wang, Y., & Zhang, M. (2024). Comprehensive Review on Fruit of *Terminalia chebula*: Traditional Uses, Phytochemistry, Pharmacology, Toxicity, and Pharmacokinetics. *Molecules*, *29*(23), 5547. <https://doi.org/10.3390/molecules29235547>
	47. Wang, C., Zhang, H., Wang, X., Wang, X., Li, X., Li, C., Wang, Y., & Zhang, M. (2024b). Comprehensive Review on Fruit of *Terminalia chebula*: Traditional Uses, Phytochemistry, Pharmacology, Toxicity, and Pharmacokinetics. *Molecules*, *29*(23), 5547. <https://doi.org/10.3390/molecules29235547>
	48. Zainab, G.A.; Haitham Mahmood, K.; Abbas, S.A. Evaluation of antimicrobial activity of ellagic acid on Methicillin-resistant Staphylococcus aureus (MRSA), Pseudomonas aeruginosa, and *Escherichia coli*. *Int. J. Health Sci.* **2022**, *6*, 11891–11899.
	49. Zhang, M.; Liu, L.; Zhao, Y.; Cao, Y.; Zhu, Y.; Han, L.; Yang, Q.; Wang, Y.; Wang, C.; Zhang, H. Discovery and evaluation of active compounds from Xuanfei Baidu formula against COVID-19 via SARS-CoV-2 M(pro). *Chin. Med.* **2023**, *18*, 94.